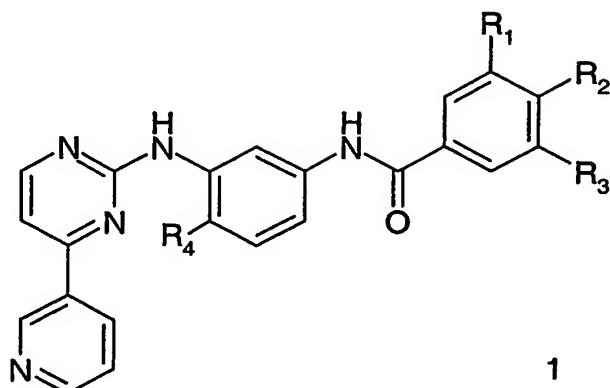


WHAT IS CLAIMED IS:

1. A compound of formula 1



wherein

$R_1$  represents hydrogen and  $R_2$  represents  $NR_5R_6$ , or  $R_1$  represents  $NR_5R_6$  and  $R_2$  represents hydrogen;

$R_3$  represents lower alkyl, fluoroalkyl, hydroxyalkyl or carbamoyl;

$R_4$  represents hydrogen, lower alkyl or halogen; and

$R_5$  and  $R_6$  represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, N-lower alkylpyrrolidinyl, or lower acyl, or  $R_5R_6$  together represent alkylene with four, five or six carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl, hydroxy or lower alkoxy;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

2. A compound of formula 1 according to claim 1 wherein

$R_1$  represents hydrogen and  $R_2$  represents  $NR_5R_6$ , or  $R_1$  represents  $NR_5R_6$  and  $R_2$  represents hydrogen;

R<sub>3</sub> represents lower alkyl, fluoroalkyl, hydroxyalkyl or carbamoyl;

R<sub>4</sub> represents lower alkyl; and

R<sub>5</sub> and R<sub>6</sub> represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, N-lower alkylpyrrolidinyl, or lower acyl, or R<sub>5</sub>R<sub>6</sub> together represent alkylene with four, five or six carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl, hydroxy or lower alkoxy;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

3. A compound of formula 1 according to claim 1 wherein

R<sub>1</sub> represents hydrogen and R<sub>2</sub> represents NR<sub>5</sub>R<sub>6</sub>, or R<sub>1</sub> represents NR<sub>5</sub>R<sub>6</sub> and R<sub>2</sub> represents hydrogen;

R<sub>3</sub> represents trifluoromethyl;

R<sub>4</sub> represents methyl; and

R<sub>5</sub> and R<sub>6</sub> represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, N-lower alkylpyrrolidinyl, or acetyl, or R<sub>5</sub>R<sub>6</sub> together represent alkylene with four, five or six carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl, hydroxy or lower alkoxy;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

4. A compound of formula 1 according to claim 1 wherein

R<sub>1</sub> represents hydrogen and R<sub>2</sub> represents NR<sub>5</sub>R<sub>6</sub>, or R<sub>1</sub> represents NR<sub>5</sub>R<sub>6</sub> and R<sub>2</sub> represents hydrogen;

R<sub>3</sub> represents trifluoromethyl;

R<sub>4</sub> represents methyl; and

R<sub>5</sub> and R<sub>6</sub> represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, or lower acyl, or R<sub>5</sub>R<sub>6</sub> together represent alkylene with four or five carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl; and a N-oxide or a pharmaceutically acceptable salt of such a compound.

5. A compound of formula 1 according to claim 1 wherein

R<sub>1</sub> represents hydrogen and R<sub>2</sub> represents NR<sub>5</sub>R<sub>6</sub>, or R<sub>1</sub> represents NR<sub>5</sub>R<sub>6</sub> and R<sub>2</sub> represents hydrogen;

R<sub>3</sub> represents trifluoromethyl;

R<sub>4</sub> represents methyl; and

R<sub>5</sub> and R<sub>6</sub> represent, independently of each other, hydrogen, lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, or lower acetyl, or R<sub>5</sub>R<sub>6</sub> together represent alkylene with four or five carbon atoms, oxa-lower alkylene with one oxygen and four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, and wherein aza-lower alkylene may be unsaturated and/or the carbon atoms of aza-lower alkylene may be substituted by lower alkyl;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

6. A compound of formula 1 according to claim 1 wherein

R<sub>1</sub> represents hydrogen and R<sub>2</sub> represents NR<sub>5</sub>R<sub>6</sub>, or R<sub>1</sub> represents NR<sub>5</sub>R<sub>6</sub> and R<sub>2</sub> represents hydrogen;

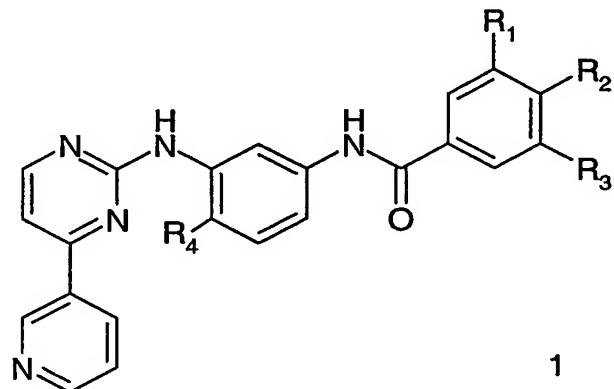
R<sub>3</sub> represents trifluoromethyl;

R<sub>4</sub> represents methyl; and

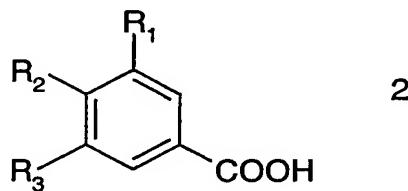
R<sub>5</sub> and R<sub>6</sub> represent, independently of each other, hydrogen, methyl, ethyl, 2-dimethylaminoethyl, 4-methyl-1-piperidinyl, or acetyl, or NR<sub>5</sub>R<sub>6</sub> together represent pyrrolidino,

piperidino, morpholino, N-methylpiperazino, 1H-imidazolyl, 1H-2-methylimidazolyl, 1H-4-methylimidazolyl or 1H-2,4-dimethylimidazolyl;  
and a N-oxide or a pharmaceutically acceptable salt of such a compound.

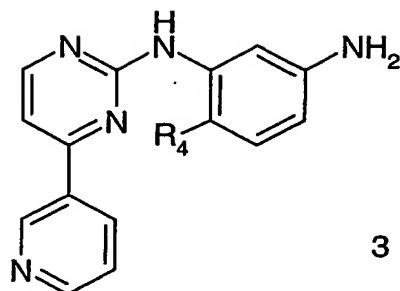
7. A process for the synthesis of a compound of the formula 1



or an N-oxide or a salt thereof, wherein the symbols R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are as defined in claim 1, characterized in that a compound of formula 2



wherein R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are as defined for a compound of formula 1, or a derivative thereof wherein the carboxy group -COOH is in activated form, is reacted with an amine of the formula 3



wherein R<sub>4</sub> is as defined for a compound of the formula 1, optionally in the presence of a dehydrating agent and an inert base and/or a suitable catalyst, and optionally in the presence of an inert solvent;

where the above starting compounds of formula 2 and 3 may also be present with functional groups in protected form if necessary and/or in the form of salts, provided a salt-forming group is present and the reaction in salt form is possible;

any protecting groups in a protected derivative of a compound of the formula 1 are removed;

and, if so desired, an obtainable compound of formula 1 is converted into another compound of formula 1 or a N-oxide thereof, a free compound of formula 1 is converted into a salt, an obtainable salt of a compound of formula 1 is converted into the free compound or another salt, and/or a mixture of isomeric compounds of formula 1 is separated into the individual isomers.

8. A pharmaceutical composition comprising as an active ingredient a compound of formula 1 according to claim 1 or a N-oxide or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier.

9. Use of a compound of formula 1 according to any one of claims 1 to 6 or of a N-oxide or a possible tautomer thereof or of a pharmaceutically acceptable salt of such a compound for the preparation of a pharmaceutical composition for the treatment of a disease which responds to an inhibition of protein kinase activity.

- 53 -

10. The use of a compound of formula 1 according to any one of claims 1 to 6 or of a N-oxide or a possible tautomer thereof or of a pharmaceutically acceptable salt of such a compound in the treatment of a disease, which responds to an inhibition of protein kinase activity.
11. A method for the treatment of a disease which responds to an inhibition of protein kinase activity, which comprises administering a compound of formula 1 according to claim 1 or a N-oxide or a pharmaceutically acceptable salt thereof.
12. Use or method according to any one of claims 9 to 11 wherein the disease is a neoplastic disease.
13. Use or method according to any one of claims 9 to 11 wherein the disease is a leukemia which responds to an inhibition of the Raf and/or Abl tyrosine kinase activity.